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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,324	07/08/2003	Norikazu Ueyama	OKA-0209	7360
23353	7590	07/31/2006	EXAMINER	
RADER FISHMAN & GRAUER PLLC LION BUILDING 1233 20TH STREET N.W., SUITE 501 WASHINGTON, DC 20036				SRIVASTAVA, KAILASH C
ART UNIT		PAPER NUMBER		
		1655		

DATE MAILED: 07/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/614,324	UEYAMA ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Dr. Kailash C. Srivastava	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 26 May 2006.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-5 and 7-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-5 and 7-21 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                     | Paper No(s)/Mail Date. _____ .  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|  | 6) <input type="checkbox"/> Other: _____ .                                  |

## **DETAILED ACTION**

1. Applicants' amendment and response filed 16 May 2006 to Office Action mailed 16 November 2005 is acknowledged and entered. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office action.

2. Your application under prosecution at the United States Patent and Trademark Office (i.e., USPTO) is assigned to Dr. Kailash C. Srivastava in Art Unit 1655. To aid in correlating any papers for this application (i.e., USSN 10/614,324), all further correspondence regarding this application should be directed to Examiner Kailash C. Srivastava in Art Unit 1655.

3. Examiner very much appreciates that the applicants label each page of the response referred above with Serial Number of the Non-Provisional U.S. Application, the Attorney Docket Number and date of amendment/response. This practice in itself immensely ameliorates the chances of papers lost during transaction/transmission of paper once a filing/response arrives at the United States Patent and Trademark Office (i.e., USPTO). However, after a response/filing arrives at the USPTO, the claims, remarks, amendments etc., are separated for proper coding to scan them in the electronic file wrapper (i.e., IFW). In order to ensure that all the papers pertaining to a particular application are properly coded and placed in the same application electronic file wrapper, and to further facilitate the prosecution; especially during a telephonic conversation/ interview with applicant/applicants' representative, Examiner suggests that applicants recite in addition to citing the information they already have in the header of the each page for any filing/response/amendment, the following information:

- a. Filing date for said application;
- b. First Applicant' s name;
- c. Group Art Unit Number (e.g., 1655);
- d. Examiner' s name (e.g., Dr. Kailash C. Srivastava); and
- e. Document Page number (e.g., Page 1);

Papers/responses filed according to above-stated guidelines immensely ameliorate the chances of papers lost during transaction/transmission, coding, indexing and placing the papers in IFW.

4. In view of applicants' amendment and arguments presented in response filed 16 May 2006 to Non-Final Office Action mailed 16 November 2005, Examiner hereby withdraws rejections to:

- Claims 1-16 under 35 U.S.C. §112, second paragraph;
- Anticipatory rejections to Claims 1-2 under 35 U.S.C. §102 (b) as being anticipated by Gariepy (WO 93/23425, 1993); and,
- Anticipatory/Obviousness rejection to Claims 1-16 under 35 U.S.C. §102 (b) as being anticipated by or, in the alternative, under 35 U.S.C. §103 (a) as obvious over Anderson et al. (U.S. Patent 5,439,829)

in the Office Action cited *supra*.

## CLAIMS STATUS

5. Claims 17-21 have been added.
6. Claim 6 has been cancelled.
7. Claims 1-2, 7-8 and 11-12 have been amended.
8. Claims 1-5, and 7-21 are pending and are examined on merits.

## Objection To Specification

9. The specification is objected to because Line one of first page of specification, in its present form does not properly cite the application priority data. Applicants are required to indicate at the first line of the first page of the specification that the instant application claims priority to a foreign application, as follows:

" This application claims priority to Japan 2002-204864 filed 12 July 2002 NO."

## *Claim Rejections Under 35 U.S.C. § 103(a)*

10. Claims 1-5, 7-16 and newly presented Claims 17-21 are rejected under 35 U.S.C. § 103 (a) as obvious over the combined teachings from Gariepy (WO 93/23425, 1993) in view of Anderson et al. (U.S. Patent 5,439,829) and further in view of Liao et al (Journal of American Society for Mass Spectrometry, Volume 8, Pages 501-509, 1997).

Claims recite a composition comprising metal complexes having functional groups, wherein said complex is attached to either N- or C- terminus of a protein or peptide through a co-va lent bond and the functional group is not cleaved in a stage of ionization in mass spectrometry. SAAID metal complex has a mono or poly-dentate ligand. Said metal complex is comprised of transition or non-transition metals and has a coordination number in the range of 2-6. Claims further are drawn to a reagent and to a method to determine the amino acid sequence of a protein, wherein the reagent and the method utilize the metal complex covalently bound to the N- or C-terminus of a peptide or a protein.

Gariepy teaches a chelating metal complex with a peptide (see amended Claims 1-10), said complex having following attributions:

- i. Having a carboxy-terminal portion comprising 3-6 amino acids;
- ii. amino acid residues adjacent to C- terminus having a reactive group for selectively and only in one direction coupling said peptide to a target molecule peptide;
- iii. branched N-terminal constituted of 4-16 amino acids to which are coupled polydentate ligands;
- iv. the reactive group of said peptide is an activated ester.

Gariepy, however, does not teach a covalent bond or that functional group is not cleaved in a stage of ionization in mass spectrometry.

Anderson et al., teaches an analogous metal complex, wherein a chelating agent is covalently bonded to a bioactive molecule (e.g., an antibody, enzyme), wherein the bioactive molecule is contacted with a support comprising a bound transition metal, wherein the metal ion in turn is chelated by the chelating agent. Anderson et al. further teach that the oxidation state of said metal ion is charged according to the reagent with which it is treated (i.e., oxidizing or reducing agent). In said complex the transition metal ion is one among: Co<sup>2+</sup>, Cr<sup>2+</sup>, or Ru<sup>3+</sup> and the oxidation of said metal ion is changed to Co<sup>3+</sup>, Cr<sup>3+</sup> or Ru<sup>2+</sup> respectively. Anderson et al. also teach that the chelating agent is one among: iminodiacetic acid, nitrilotriacetic acid, terpyridine, bipyridine, triethylenetetramine, biethylenetriamine and 1,4,7 triazacyclonane (Abstract and Column 8, Lines 9-21). Anderson et al. also teach the following:

- v. preparing bidentate, tridentate, quadridentate ligands (Column 6, Lines 50-53);
- vi. functional groups that form the covalent bonds with amino acid at N-terminus;
- vii. nucleotides and ester forming groups;
- viii. teach chemical formulae having identical or analogous compounds to those claimed instantly (See for e.g., Column 8, Lines 22-68; Column 9, Lines 1-61; Column 77, Lines 28-60 and Column 78, Lines 28-33 and 45-56);
- ix. reagents comprising a metal complex that is identical or similar to the instantly claimed metal complex (Column 77, Lines 28-60, Column 78, Lines 28-30); and
- x. methods employing metal complex comprising reagents for assays (Column 78, Lines 28-33 and 45-56) and protein sequencing protocols.

Despite explicitly not teaching that in and of itself the oxidation state of a metal is changed, as pointed out above, Anderson et al. teach metal ions with different oxidation states and that the oxidation state for said ion is changed. Thus, intrinsically Anderson et al also teach the coordination number to be within the range claimed instantly.

Liao et al teach “ when a charged group is attached to the N-terminus of a peptide, “ Matrix-Assisted Laser Desorption Ionization (i.e., MALDI) spectrometry spectra provide a powerful tool to initially and rapidly determine the structure” (Page 508, Column 2, Lines because reactions through which fragment ions are formed are fundamentally different than those in which protonated peptides are the precursor ions.

It would have been *prima faciae* obvious to one of ordinary skill in the art at the time the invention was made to modify Gariepy’ s composition according to the combined teachings from Anderson et al. and Liao et al. to obtain a composition comprising a metal ion complex covalently bonded to C- or, N-terminus of a protein or a peptide to make a reagent and to apply said composition and reagent in a method to determine the amino acid sequence of a protein/ peptide; because Anderson et al. teach the production, composition and reagent comprising said metal ion complex with different coordination numbers for said metal ions, wherein said complex is chelated , has mono- or multi-dentated ligands and is bonded to said c- or N-terminus of a peptide/protein and to determine amino acid sequence of a peptide/protein, while Liao et al teach that said bonds are not cleaved in a MALDI spectrometry.

Thus, an artisan of ordinary skill, at the time that said invention was made would be motivated to combine the teachings from each one of the cited references to develop a composition, reagent and a method to determine the amino acid sequence of a peptide/protein applying said composition/reagent as discussed above.

From the teachings of the references cited supra, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### ***Claim Rejections – 35 U.S.C. § 112***

#### ***Second Paragraph Rejections***

11. Claims 1-5 and 7-16 and newly presented Claims 17-21 are rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter, which applicants regard as the invention.

- Recitation, “ which is to form” in each one of Claims 1-2, 7-8, 11-12, 17, 19 and 21 renders those claims vague, unclear and therefore indefinite because the phrase “ which is to form” in and by itself denotes a futuristic event. The metes and bounds of the claimed subject matter are not clearly defined. The examiner suggests that the applicants define the metes and bounds of the phrase “ which is to form” .
- The recitation, “ derivative” in claim 21 renders said claim unclear as well as confusing, and therefore indefinite because this term does not clearly define as to how similar a compound should be of the base compound to be called derivative, i.e. the term does not define the metes and bounds of the claimed subject matter. Applicants need to define the metes and bounds of the recitation, “ derivative” .

### **CONCLUSION**

12. For aforementioned reasons no Claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Terry McKelvey, can be reached on (571)-272-0775 Monday through Friday, 8:30 A.M. to 5:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). Alternatively, status inquiries should be directed to the receptionist whose telephone number is (703) 308-0196.

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July 23, 2006

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